Specialty Conference

Moderator

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Discussants

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Infectious Disease Emergencies

PART IV:

Patients Presenting with Gastrointestinal Disorders

PHYLLIS OILL, MD:* This part of the symposium on Infectious Disease Emergencies is concerned with those infectious processes that primarily are referable to the gastrointestinal tract. Dr. Stephan Targan will discuss the infectious diarrheal syndromes associated with dehydration and electrolyte abnormalities. Dr. Norman Panitch will then speak about mediastinitis and peritonitis. Table IV-1 is a compilation of the infectious disease entities that are related to this area of discussion.

Infectious Diarrheal Emergencies

STEPHAN TARGAN, MD:† The difficulty in infectious diarrheal syndromes is to identify which diseases require urgent versus nonemergent management. For example, in a dehydrated patient with a history of diarrhea, the decision will be whether to act immediately to reverse a potentially fatal illness, or if the disease process is self-limiting, to allow the patient to heal himself and not to intervene. With a patient who presents in shock with a history of diarrhea, the immediate fluid replacement therapy is obvious; however, knowing which patients need further rapid evaluation and further additional treatment is not always as apparent.

In order to be prepared to manage true emergencies, physicians must be familiar with both the emergent and nonemergent infectious diarrheas. The discussion will begin by focusing on how the various types of infectious diarrhea and dysentery clinically present and how one can attempt to rapidly differentiate them by: (1) obtaining appropriate historical information; (2) knowledge of presenting signs and symptoms, and (3) use of proctoscopy and studies of stool specimens. With these facts established, I will then discuss which illnesses require immediate therapy or admission to hospital (or both), the appropriate therapy and which disease entities can be managed in a less acute manner by limited diagnostic and therapeutic manipulations to the patient. An in-depth discussion of each of these diarrheal syndromes is beyond the scope of this paper.

A normal person excretes approximately 1.7

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TABLE IV-1.—*Infectious Diseases Presenting with Gastrointestinal Symptomatology*

Diarrhea secondary to toxin production
Staphylococcus aureus
Escherichia coli (E. coli)
Clostridium perfringens (C. perfringens)
Vibrio cholerae (V. cholerae)
Diarrhea and dysentery
Shigella
E. coli
Salmonella typhi (typhosa)
Staphylococcal enterocolitis
Pseudomembranous colitis secondary to antibiotic therapy
Bloody diarrhea and dysentery
Entamoeba histolytica
Shigella
Acute mediastinitis secondary to esophageal perforation
Peritonitis
Primary (spontaneous) peritonitis
Nephrosis
Alcoholic cirrhosis
Tuberculosis
Fungal
Secondary peritonitis
Bile
Bacterial
Intraabdominal abscess
Gastrointestinal perforation
Alteration of intestinal wall permeability (i.e. intestinal obstruction, volvulus, intussusception, ischemia)

percent or between 150 to 200 ml of the 9 to 10 liters of gastrointestinal secretions produced per day. Eighty percent of this is usually absorbed by the small intestine and another 18 percent by the colon.[1] If the bowel secretes an increased amount of fluid with an increased transit time to overwhelm these very efficient mechanisms, or these absorptive mechanisms are inhibited by various agents, an increased amount of fluid is excreted and diarrhea results. There may be a pronounced variation in the electrolyte composition of the stool water which depends on the level of the gastrointestinal tract that the diarrhea develops and the rapidity of the resultant transit time. Most types of infectious diarrhea yield large amounts of sodium, chloride and bicarbonate loss or a small bowel fluid. However, when dysentery or colonic mucosal sloughing with loss of erythrocytes, leukocytes and cellular debris occurs, in addition to a small bowel diarrhea, there is also loss of protein with various additional electrolyte combinations.[1]

Diagnosis

In order to understand how to differentiate the presentations of the infectious diarrheas and dysenteries, it is helpful to have a general concept of the various pathological mechanisms. There are three basic mechanisms.[2,3]

- *Type I* is toxigenic, or an exotoxin which is produced by a replicating bacteria either in an external medium or in the intestinal milieu which causes profuse efflux of fluid and electrolytes from the small bowel.[4]
- *Type II* is superficial, longitudinally progressive colonic invasion of the mucosa by a pathogen producing both a watery diarrhea and dysentery.[5]
- *Type III* is a deep and localized penetration of both the ileal and colonic mucosas usually producing diarrhea and dysentery, but in addition systemic and toxic symptoms.[6]

Although many of the following diarrhea syndromes have classical presentations, often the patients will have history of prior diagnostic manipulation or therapy, or both, which may modify the susceptibility, presenting manifestations or severity of illness in the affected person. The following are important general questions to ask: (1) Has the patient had prior gastric surgical operation or a natural hypoacidity state? Since acid in the stomach provides a barrier to bacterial invasion, the absence of this could enable invasion and infection of the more distal gastrointestinal tract to occur with a lesser inoculum of certain pathogenic bacteria.[7-11] This could alter epidemiological histories and make them less exacting. (2) Has the patient had prior antibiotics? This type of information could provide a clue as to the cause of various syndromes which follow antibiotic use. In addition, since the products from natural intestinal bacterial flora, particularly anaerobes, act as a growth suppressant to invading pathogenic bacteria, prior therapy of antibiotics could alter the onset and duration of symptoms of certain bacterial diarrheas.[3,12-17] (3) Has the patient's rapid transit time been altered with opiates or anticholinergics, or both? Diarrhea and rapid transit time are usually protective defense mechanisms by the host to rid itself of the invading pathogen. Treatment with anticholinergic agents has been shown to exacerbate and worsen the symptoms of certain diarrheas.[2] This occurs by either enabling greater contact time between the mucosa and invading organism which increases its pathogenicity, or by the development of toxic dilation of the bowel.

Although there are tremendous overlaps between how the various infectious causes present,[2] and a spectrum of symptomatology does occur

TABLE IV-2.—*Type I: Diarrhea Secondary to Toxin Production*

Pathogen	*History*	*Presenting Clues*	*Systemic Symptoms*	*Stool Exam*
Staphylococcus aureus ...	Ingestion of foods, dairy products	Acute onset 4-8 hrs, vomiting, diarrhea (severe)	Minimal	No leukocytes
Escherichia coli	Travel	Onset 24-72 hrs, no vomiting, diarrhea (moderate)	Minimal	No leukocytes
Clostridium perfringens ..	Contaminated food, cooked meat	Onset 12-24 hrs, vomiting (±), abdominal pain (severe), diarrhea (moderate)	Minimal	No leukocytes
Vibrio cholerae	Endemic and epidemic	Onset 24-72 hrs, diarrhea (severe, "rice-water")	Hypokalemic nephropathy	No leukocytes

with each disease, some general guidelines can be made which may be useful. Since we are concerned with emergencies in this symposium, the most severe presenting manifestations will be discussed.

Type I Diarrheal Syndromes

Patients presenting with diarrhea in the absence of systemic complaints are usually suffering from one of several toxigenic types of diarrhea (Table IV-2). These are commonly of acute onset with minimal symptoms, other than general malaise usually secondary to large fluid efflux into the bowel.[3,4,18] Invariably, methylene blue staining of fresh stool specimens shows no leukocytes. Inference as to the type of toxin incriminated can be made from the history and certain presenting signs.

Staphylococcal toxin is usually produced in an external medium consisting of dairy products and baked goods, such as Boston cream pie. The incubation period is short, four to eight hours, because no bacterial growth is required in the gastrointestinal tract for toxin production. As compared with other toxins,[18] a severe amount of vomiting with an abrupt explosive diarrhea results. Escherichia coli toxin is produced in the bowel by a toxigenic strain and can be acquired as "travelers diarrhea" or endemically in "child nursery" populations. The onset is not as acute as staphylococcal disease since toxin production is dependent on proliferation within the gut. It has a fairly short incubation period of up to 48 hours.[19,20] Clostridia perfringens toxin is produced by the organism in poorly cooked meats, canned vegetables and fruits, that is, situations in which there is a lack of killing of spores. This particular toxin can produce severe abdominal pain along with a profuse diarrhea.[16,20] Vibrio cholerae is rarely isolated in this country; however, a history of endemic travel exposure and return to this country can be helpful to consider this pathogen's toxin as a possible cause of diarrhea.

Type II Diarrheal Syndromes

Patients who present with diarrhea *and* dysentery (by history or findings on tests of stool specimens) usually have some systemic symptoms, along with tremendous fluid and mucosal cell loss. On studies of stool specimens in all of these patients the presence of leukocytes will be noted. Occasionally (as discussed below), certain specific differences in the fecal leukocyte evaluation can be helpful in differentiating causes. However, the most helpful clues are differentiating historical and presenting symptomatology (Table IV-3).

Shigella can be transmitted with as few as 10 to 100 organisms.[16] A history of working with, or exposure to, personnel or patients in nursing homes where the organism is endemic is helpful to establish the person-to-person transmission of this disease. In addition, a history of recent travel to Mexico or South America should also raise the possibility of Shigella dysentery. In about 50 percent of the cases, some bloody diarrhea occurs. There is some abdominal pain; however, it is not as severe as with clostridial disease. The illness can present with progressive upper to lower gastrointestinal symptoms, such as nausea which then progresses to tenesmus, which is characteristic of the type II pathogenic mechanism. Systemic symptoms such as meningismus, seizures, upper respiratory symptoms and rhabdomyolysis do occur. Occasionally, bacteremias and septicemia with fever can occur, but are not the rule.[21]

Penetrating E. coli has no distinguishing historical characteristics. Its presentation is similar to Shigella, with findings on tests of stool also showing polymorphonuclear leukocytes.[22] These latter two entities can be only distinguished by (1) isolation of Shigella from stool culture and

(2) showing the presence of a toxigenic strain of E. coli from feces.

Salmonella dysentery, or nontyphoid Salmonella, requires 10^5 to 10^8 organisms to produce disease. The important historical clues are ingestion of egg products, poultry and the use of possibly contaminated water supplies. There is occasional bacteremia with fever, but this is the exception. On examination of stool specimens, many leukocytes are found with usually greater than 70 percent of them polymorphonuclear.[16]

Salmonella typhi or paratyphi can present initially similarly to Salmonella dysentery. The history, if positive, more classically shows there to have been endemic travel to Mexico or contact with contaminated water or food supplies. These patients can present with a multitude of systemic complaints, such as headache, cough, pharyngitis and abdominal tenderness. The patients can be in a toxic condition, with high fevers and prostration, indicative of bacteremia. Although diarrhea can be profuse, constipation can, at first, be the predominant gastrointestinal symptom. Examination of stool specimens for leukocytes can be helpful in that of all the types of dysentery, Salmonella typhi usually presents with greater than 70 percent mononuclear leukocytes. Although leukopenia and bradycardia are classically reported in typhoid, it is transient and often difficult to document.[23]

Staphylococcal enterocolitis is a true emergency where prompt diagnosis is mandatory. A history of recent antibiotic use or surgical operation, or both, is the usual predetermining factor. These patients are the ones who are most likely to present with shock with no evident prior diarrhea. Studies of stool with methylene blue or Gram stain will show many leukocytes and sheets of staphylococci. This is a specific differential point which should stimulate immediate therapy.[24,25]

Pseudomembranous enterocolitis presents following initiation of administration of antibiotics. The most common implicated have been clindamycin and lincomycin, with a few cases secondary to tetracycline and ampicillin.[26] The onset of diarrhea can occur from one day to two weeks after therapy is begun. This can present with tremendous fluid loss and toxic megacolon. Leukocytes will be shown on examination of stool and proctoscopy is necessary to differentiate this entity,

TABLE IV-3.—*Type II: Diarrhea and Dysentery*

Pathogen	*History*	*Presenting Clues*	*Systemic Symptoms*	*Stool Exam*
Shigella	Endemic; nursing home; recent travel—Mexico, South America	Bloody diarrhea (60%); abdominal pain; progressive symptoms; tenesmus	Seizures; meningismus; occasional bacteremia; fever; respiratory symptoms	Polys*; 1+ red blood cells; no organisms
Escherichia coli	Travel history	Above plus abdominal pain	Variable	Polys, ± red blood cells
Nontyphoid Salmonella	Prepared foods; poultry; egg products	"Greenish stool" or watery stool	Fever; occasional bacteremia	70% polys; 30% mononuclear cells
Salmonella typhi	Water supplies; food handling	Constipation first; headache; upper respiratory infection; "leukopenia-bradycardia"	Elevated temperature (spiking); toxic symptoms	70% mononuclear cells; 30% polys
Staphylococcus aureus (enterocolitis)	Prior antibiotics	Severe dehydration leading to shock	Comatose	Sheets of staphylococci + leukocytes
Pseudomembranous (enterocolitis)	Clindamycin; other antibiotics	Classic ulcers on proctoscopy	Minimal	+ leukocytes

*Polymorphonuclear cells

TABLE IV-4.—*Type III: Bloody Diarrhea*

Pathogen	*History*	*Presenting Clues*	*Systemic Symptoms*	*Stool Exam*
Entamoeba histolytica .	Mideast; Mexico	Few abdominal signs; toxemia; peritonitis; 20-30 bowel movements/day (can be *watery*); tenesmus; *ulcers* on proctoscopy; abdominal mass	Malaise	+ leukocytes; + wet mount; + Schaudin's prep
Shigella	USA; travel	Prolonged course (>5-7 days)	Malaise	+leukocytes
Shiga bacillus	Rare in the USA; travel	Toxic; fluid loss	Dehydration	Leukocytes; red blood cells

having classical pseudomembranes on the mucosa, from other modified dysenteries, or particularly staphylococcal enterocolitis.[26,27]

Type III Diarrheal Syndromes

In patients who present with predominantly bloody diarrhea, and appear either acutely ill or in a toxic condition, usually there is one of two infectious causes (Table IV-4). The presentation and severity of amoebic colitis is quite variable, but what will be described here is the most severe type. These patients can present with chronic diarrhea with an acute exacerbation, or the initial symptomatology may be the rapid onset of watery diarrhea. A travel history to Mexico or the Middle East, if positive, can be helpful. Usually the patient has some tenesmus and can have peritoneal signs or abdominal mass, or both. On examination of stool, motile amoeba on heated wet mount may be shown, but proctoscopy with several Schaudin's preparations is a must. A diagnosis is made by seeing the ulcerations on colonic examination with the presence of amoeba shown on a smear.[28]

Shigellosis, particularly with the Shiga bacillus (Shigella dysenteriae) as the etiologic agent, can have a prolonged course and patients may be in a toxic condition and have bloody diarrhea. Recent travel history to endemic areas, such as India and Pakistan or Mexico, should be elicited from patients. Generally, the conditions of these patients are not as toxic as in patients with amoebic disease. Study of stool specimens might be helpful in differentiating these two diseases if there is a lack of amoeba seen. However, culture gives the definitive diagnostic clue.

If none of the above is revealing, other more chronic forms of noninfectious bloody diarrheas —such as ulcerative colitis, ischemic colitis or vasculitis—should be considered as diagnostic possibilities. As a helpful review, Tables IV-5 and IV-6 list the major historical data and certain presenting signs and symptoms most commonly associated with specific etiological agents causing diarrhea.

TABLE IV-5.—*Major Historical Data*

Major Historical Point	*Pathogen*
Travel	Escherichia coli Entamoeba histolytica Vibrio cholerae Shigella
Antibiotics	Staphylococcal enterocolitis; pseudomembranous
Dairy products; baked goods	Salmonella (nontyphoid) Staphylococcal toxin
Water supplies "closed"	Salmonella typhosa
Meat and canned goods	Clostridium perfringens

TABLE IV-6.—*Major Presenting Symptom or Sign*

Major Sign or Symptom	*Pathogen*
Vomiting	Staphylococcus aureus (toxin); Salmonella
Shock (alone) with diarrhea	Staphylococcus aureus (enterocolitis)
Elevated temperature	Salmonella typhi Entamoeba histolytica Shigella
Abdominal pain (general)	Entamoeba histolytica Clostridium perfringens Escherichia coli (toxin)
Tenesmus	Escherichia coli (penetrating); Shigella; Entamoeba histolytica
Systemic-toxic	Salmonella typhi Entamoeba histolytica (colitis)
"Appendicitis"	Salmonella typhi

Therapy

A useful therapeutic approach is to be aware of the mode of presentation and natural course of the various types of diarrhea. This will aid in instituting necessary treatment and conversely, avoiding unnecessary therapeutic approaches. Table IV-7 lists the modes of presentations with their most likely etiologic agents. The clinical presentations can be characterized as follows:

- Acute and fulminant onset with progressive course, sometimes rapid.
- Acute and often fulminant presentation, with a self-limited course.
- Chronic mode of presentation with an acute exacerbation and often fulminant course.

Using these groups as guidelines for therapy, a review of therapeutic maneuvers with prognostic evaluation will be discussed. The first group of diseases with rapid onset are usually rapidly progressive and there should be immediate admission to hospital or intervention, or both, for patients affected (Group A, Table IV-7).

When the diagnosis of toxic amoebic colitis is made from the criteria stated above there should be immediate admission to hospital with fluid replacement and therapy with antiamoebic drugs should be started. Those drugs should be either

TABLE IV-7.—*Clinical Course and Most Common Cause in Diarrheal-Dehydration Syndromes*

Group A: Acute fulminating and rapidly progressive
Amoebic colitis
Staphylococcal enterocolitis
Vibrio cholerae
"Pseudomembranous enterocolitis"
Group B: Acute fulminating and self-limited
Toxic—staphylococcal
Escherichia coli (toxigenic)
Clostridium perfringens
"Shigella" toxin
Salmonella dysentery
Shigella dysentery
Escherichia coli
Group C: Chronic-acute exacerbation fulminant
Amoebic colitis
Salmonella typhi

metronidazole (750 mg given orally three times a day for 10 to 14 days) or combinations of emetine (1 mg per kg of body weight given intramuscularly), chloroquine (250 mg given four times per day for 2 days, then twice a day for 12 days) and diiodohydroxyquin (650 mg given three times a day for 21 days). If peritoneal signs, some hypotension, fever and a toxic condition are present, a physician should only wait 12 to 24 hours to see if there is improvement with supportive and chemotherapeutic approaches before deciding whether to intervene surgically. There is a high mortality from perforation and toxic megacolon with the severe form of this disease entity and, therefore, use of anticholinergics is to be avoided. The prognosis, even with surgical intervention, is very poor.[28]

Once staphylococcal enterocolitis is diagnosed from findings on studies of stool specimens, blood cultures should be made, a central venous line should be inserted and vigorous fluid replacement begun to maintain adequate circulating volume. Chemotherapy with vancomycin, 2 grams given orally per day (these are usually penicillin-resistant staphylococci) and 2 grams given intravenously, should be begun.[29] The fluid loss may be enormous and may last several days to weeks. However, clinical response can occur much earlier in the course with rapid appropriate therapy. The prognosis is poor, but it is extremely important to persist with therapy.[24,25,29]

After proctoscopic evaluation and diagnosis of pseudomembranous enterocolitis, the insighting agent should be discontinued immediately. The patient is admitted to hospital to correct any dehydration, and closely observed for any signs of toxic megacolon or perforations. Anticholinergics, such as diphenoxylate hydrochloride with atropine sulfate (Lomotil®), must be avoided as they can increase the possibility of these complications. Reversibility of diarrhea should be expected to occur between two and five days after discontinuation of therapy with antibiotics.[26,27] The prognosis is good if the disease is diagnosed early. However, up to a 26 percent mortality from this disease has been reported and therefore the importance of early recognition must be stressed.[27]

Although it is rare, when diarrhea due to Vibrio cholerae is diagnosed, the patient should be admitted to hospital and treated with either orally given electrolyte solutions containing glucose or intravenously given electrolyte fluids. Since there is usually only an increased efflux of fluids and electrolytes produced by the toxin, and the absorptive mechanism remains intact in the small bowel, oral treatment is possible.[4,11,20] In addition, orally administered tetracycline decreases the duration and severity of the illness. Future therapy may include using antiprostaglandin compound, indomethacin. There is evidence suggesting that prostaglandins might be an intermediary agent that increases the stimulation of adenylcyclase production by this toxin.[20] Stimulation of adenylcyclase increases the efflux of fluid from the bowel.

Those entities that can present acutely and similarly to the above illnesses, but are self-limited (Group B, Table IV-7), usually do not require that the patient be admitted to hospital and demand restraint from the physician as to vigorous therapy.

Toxic types of diarrhea are self-limited and commonly require only oral fluid support. The course can be up to a maximum of 36 hours before resolution. Any persistence of diarrhea beyond that time requires reevaluation as to an alternative cause. Occasionally admission to hospital is required for fluid replacement. Short courses of anticholinergics can help relieve symptoms without exacerbating the course.[4,11,16,18]

When the diagnosis of dysentery due to Salmonella is made, no therapy is usually needed. Fluid support and reassurance is most helpful. Antibiotic therapy is generally not indicated (unless patients appear septic or are bacteremic) since it may potentiate carrier states and possibly prolong the illness.[17,30] Diarrhea generally lasts three to five days and reevaluation is indicated if symptoms persist beyond this point. Brief courses of anticholinergics have been used but they should

be avoided so as to minimize prolongation of illness.[16]

Shigellosis that patients acquire in the United States or Mexico has an acute onset, but is generally a self-limited disease. Admission to hospital is usually not required, although with persistent diarrhea, dehydration and toxic symptoms, this occasionally becomes necessary. Fluid support is the most important treatment method. Home enteric isolation should be instituted because of the extremely small inoculum required for transmission of the disease. Use of anticholinergics is to be avoided at all times because they increase the symptoms and duration of illness.[16] If admission to hospital is required, ampicillin or tetracycline therapy is suggested. Antibiotic treatment also should be considered for outpatients if diarrhea persists beyond the usual five days.[21]

At times, certain diarrheal syndromes will present with a long indolent, benign course with a superimposed acute exacerbation, which requires therapeutic intervention (Group C, Table IV-7). For example, in a patient infested with amoeba there can be a chronic period of mild symptoms, then the condition can acutely exacerbate and the patient present to the physician with the identical clinical features as in those persons with the primary acute disease. The same diagnostic and therapeutic guidelines are still relevant and apply to these patients.

Salmonella typhosa is another pathogen causing infectious diarrhea that can have a chronic course with undulating fevers and symptoms. A patient with this prior history may present with toxic symptoms, severe diarrhea and dysentery. After making the diagnosis from results of appropriate cultures (blood, urine, stool or bone marrow), the patient should be admitted to hospital, treated with fluids and antibiotics and observed for possible small bowel perforation.[16] The antibiotics of choice are parenterally given chloramphenicol or ampicillin continued until patients are afebrile for at least five to seven days. Because an increasing number of isolates from Mexico are resistant to chloramphenicol, patients from this geographic area should be treated initially with ampicillin.[31] Generally, some clinical response will be observed within five days; however, if symptoms persist, the possibility of antibiotic resistance must be considered and confirmed by *in vitro* susceptibility studies. Besides chloramphenicol and ampicillin, trimethoprim-sulfamethoxazole is another effective agent against most strains of S. typhosa and can be used as an alternative drug. Additionally, persistence of symptoms may be secondary to peripheral focal disease, such as sequestered abscess, osteomyelitis or cholecystitis. A careful and extensive evaluation for these potential sources of persistent bacteremia must be instituted.

Acute Mediastinitis

NORMAN PANITCH, MD:* Perhaps in the 1970's it is appropriate for a clinical gastroenterologist to discuss the syndrome of acute mediastinitis. Acute mediastinitis was at one time a prevalent disorder. Before the advent of modern culture techniques and potent antibiotics, bacterial infections within the neck, lung, pleura and vertebrae would tend to spread along available fascial planes and invade the mediastinum. In the 1970's, because of the easy availability of upper gastrointestinal endoscopy, esophageal dilatation and high speed ballistics, acute mediastinitis is almost always secondary to some condition that has resulted in esophageal perforation.

Anatomic and Bacteriologic Considerations

The mediastinum is a potential extrapleural space which communicates with other potential spaces of the chest and neck. Infections involving the pretracheal space arise from perforations of the anterior wall of the esophagus as well as from the spread of infections from the lateral pharyngeal spaces and the pyriform fossae. The above infections may then spread into the mediastinum. Posterior perforations of the cervical esophagus involve the retrovisceral space. The latter is the most common mode of spread of infection into the mediastinum since most perforations in the cervical esophagus traverse the posterior wall. The upper two thirds of the thoracic esophagus lie to the right of the midline and, consequently, perforations here would tend to lead to right pleural effusions, whereas the lower third of the thoracic esophagus curves gently to the left of the midline. Perforations of the distal esophagus, therefore, lead to associated left pleural involvement. Respiratory dynamics appear to influence the spread of inflammation into the mediastinum. Negative intrathoracic pressure will tend to attract irritative oral and gastric contents into the mediastinum resulting in chemical mediastinitis. The esophagus, like the rest of the upper gastrointestinal tract, derives its microflora from the mouth.

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TABLE IV-8.—*Acute Mediastinitis—Etiologic Factors*

Esophageal Perforation
Instrumental
Noninstrumental
Postemetic
Foreign body
External trauma
Neoplasm
Caustic ingestion
Infections of Adjacent Structures
Lung and pleura
Subphrenic extension
Osteomyelitis

The microflora of the esophagus is scanty, a mixture of aerobic and anaerobic organisms and as a rule is penicillin sensitive.

Etiologic Factors[32] (see Table IV-8)

Perforations of the esophagus are infrequent but catastrophic when they occur.[33] They can occur secondary to *external trauma* such as gunshot wounds and stabbings, or may be seen following *internal trauma,* as with sharp foreign bodies, caustic ingestions and instrumentation, or may occur spontaneously. The diagnosis is usually suspected after a brief history or physical examination. The latter shows supraclavicular or subcutaneous crepitations. Pleural effusions can develop if the thoracic or distal esophagus has been perforated. On x-ray films of the chest, pneumomediastinum, pneumothorax, hydropneumothorax or subcutaneous emphysema may be seen. An esophagram using a water soluble medium is frequently helpful in delineating the site of perforation. If the latter is negative, and the diagnosis is strongly suspected, esophagoscopy with minimal air insufflation is then recommended.

Perforation due to instrumentation. As the field of internal medicine becomes increasingly more "invasive," perforation of the esophagus secondary to instrumentation has become more prevalent. By instrumentation I mean diagnostic endoscopy, bougienage for esophageal strictures, pneumatic dilatation for achalasia and diffuse esophageal spasm and the placement of Linton and Sengstaken-Blakemore tubes in the treatment of bleeding varices. It should be noted that with flexible fiberoptic endoscopes and proper supervision, this complication has become rare at large university hospitals. At Harbor General Hospital in almost a two-year period in which about 1,000 upper gastrointestinal endoscopies have been done, there has not been a single esophageal perforation secondary to esophagoscopy.

At the time of instrument perforation, most patients will complain of immediate retrosternal pain and dysphagia. The onset of fever, leukocytosis and dyspnea heralds true mediastinitis. Once perforation has been shown to have occurred, surgical consultation should be immediately obtained. Antibiotics in high doses should be used whether or not immediate surgical operation is advised. Penicillin administered intravenously is the drug of choice. In most patients emergency surgical procedures will be required for primary repair of the perforation. Two layered closures of the esophagus are recommended along with drainage of the mediastinum. An occasional patient can be treated with local cervical drainage if the suppuration has become chronic or localized, or both.

Postemetic perforation.[34] The syndrome of spontaneous rupture of the esophagus deserves special note for it is diagnosed antemortem in only about half the cases. The first clear description of this entity was published in 1724 by Herman Boerhaave, a physician practicing in Holland. The patient, Johannes, Baron of Wassenaar, a 51-year-old admiral of the Republic and Dikereene of the Rhineland became critically ill after gorging himself on a duckling dinner and inducing emesis, which he frequently did after his debauchery. He complained of a tearing in his chest with the sudden onset of chest and back pain. He died hours later. Dr. Boerhaave, who did the autopsy, placed a needle in the left side of the patient's chest and noted the aroma of duckling. He quickly deduced that the Admiral had ruptured his esophagus.

In current series describing this entity it should be noted that in about 5 percent of patients there is no pain and in about 20 percent an x-ray film of the chest shows no abnormalities. The classic x-ray findings observed in this condition include a pneumomediastinum and a left pleural effusion. The former can sometimes be seen as a linear lucency outlining the border on the left side of the heart. The pleural effusion has a high amylase content derived from the salivary isoenzyme. Immediate use of barium or preferably maglumine diatrizoate (Gastrografin®) swallow is indicated, followed by esophagoscopy if the contrast study is negative. Once the diagnosis is confirmed, high dose penicillin therapy is instituted, hypotension is corrected with volume repletion and the patient is then taken to the operating room where a two-layered closure is carried out. Most surgeons

TABLE IV-9.—*Intestinal Microflora*

Proximal Small Intestine
Aerobes (Streptococcus, Lactobacillus, Candida)
$<10^5$/gm
Distal Small Intestine(transition zone)
Aerobes, Anaerobes
10^5-10^7/gm
Colon
Anaerobes (Bacteroides, Bifidobacterium, Peptostreptococcus); Aerobes (Escherichia coli)
10^7-10^{11}/gm

recommended a fundic patch to buttress the weakened area.

Peritonitis

The peritoneum is a serous surface with an area of about 50 percent of the external body surface. It is easy to appreciate that inflammation of a large portion of the peritoneum would result in massive fluid shifts within the abdomen. Within 24 hours, the volume within the abdomen may reach 5 to 10 liters. Inflammation also permits absorption of toxic and metabolic products. Inflammation of the peritoneum produces immediate effects upon intestinal function. Paralytic ileus and distention soon are observed. The above changes have their ultimate effects upon the cardiopulmonary system with resulting shock, respiratory and myocardial depression.

The symptoms and signs of peritonitis may be divided into two phases, *reflex* and *toxic*.[35] The reflex symptoms and signs are early and include pain, vomiting, an anxious facial expression and superficial hyperesthesia. Later, the toxic signs of abdominal distention, ileus and toxemia appear. The latter are more serious. Alterations in temperature and clinical shock may be either reflex or toxic.

In order to appreciate the bacteriology involved in peritonitis from any of the innumerable causes, we will at this point briefly review the general microflora of the gastrointestinal tract (Table IV-9). In order to initiate empirical, early antibiotic therapy before cultures are available, it is important to realize that the bowel microflora differs quantitatively and qualitatively depending upon basic anatomic location.[36] Under normal conditions, the upper small intestine has a relatively sparse, endogenous aerobic bacterial flora. The predominant organisms in the duodenum, jejunum and proximal ileum are the streptococci, Lactobacillus and the fungus, Candida albicans, at less than 10^5 organisms per gram. Significant growth of up to 10^7 organisms occurs only in the distal ileum where anaerobic bacteria begin to become numerically important. As one crosses the ileocecal valve, the flora changes dramatically. In the colon, the anaerobes predominate—that is, Bacteroides, Bifidobacterium, Peptostreptococcus and Clostridium. Anaerobes in the colon outnumber the coliforms 1,000-10,000:1. This takes on clinical importance when one considers injury to the bowel in a normal person. Colonic injuries have a rather high incidence of secondary anaerobic infection. As a rule of thumb, perforation or rupture of the large bowel must be treated with antibiotics which cover both aerobes and anaerobes, such as gentamicin and clindamycin hydrochloride, while upper intestinal injuries can be treated with penicillin alone. Chloramphenicol still remains an excellent drug in treating anaerobic infections and is an effective alternative to clindamycin. Tetracycline has been relegated to a second-line status for treating anaerobes because of the identification of resistant strains of Peptostreptococcus and Bacteroides.

Classification of Peritonitis

Peritonitis can be simply classified as being either primary or secondary. Primary peritonitis is generally due to an infectious process with bacteria being the most common pathogen. Secondary peritonitis is usually related to perforation with infection then predominating. A good rule to remember is that primary bacterial peritonitis is almost invariably *unimicrobial,* whereas secondary bacterial peritonitis (peritonitis which follows or complicates another disease or injury of the abdomenal contents) is invariably *polymicrobial.* In addition, the secondary form is characterized by bacterial flora of anaerobic predominance, whereas anaerobes are rarely, if ever, involved in primary peritonitis.

Primary or Spontaneous Peritonitis

Primary Bacterial Peritonitis of Nephrosis

The first type of primary peritonitis that we will consider is that of pneumococcal peritonitis. This disorder has become a rare disease. It is a disease of children, usually seen in young girls with nephrotic syndrome. Associated pulmonary infections are not usually noted. It is characterized by the sudden onset of fever, abdominal distention and tenderness. Vaginal smears and cultures show the presence of the pneumococcus in a mi-

TABLE IV-10.—*Spontaneous Bacterial Peritonitis of Cirrhosis*

Setting
Decompensated cirrhosis
Ascites
Portal hypertension
Signs
Fever—81 percent
"Peritoneal signs"—65 percent
Bowel sounds decreased or absent—64 percent
Hypotension—69 percent
Laboratory
Leukocytosis—72 percent
Positive blood cultures—76 percent
Abnormal liver function tests
Characteristic ascitic fluid
Ascitic Fluid
"Infected transudate" (protein <2.5 gm per 100 ml)
>250 cells per cu mm (polymorphonuclear cells)
Positive identification on Gram stain—40 percent
Single organism isolated (Escherichia coli, Pneumococci, Klebsiella, Enterococci)
Anaerobes not implicated

nority of cases. The peritoneum is found to be covered by a greenish watery exudate if laparotomy is undertaken for diagnosis. The treatment of choice is parenterally given penicillin for at least one week.

Streptococcal peritonitis, usually caused by the β-hemolytic streptococci, is also an uncommonly observed disease in the antibiotic era. It is seen in the above clinical setting and treated in a similar manner.

Spontaneous Bacterial Peritonitis of Cirrhosis (SPC)

SPC has become a relatively common entity. It has a reported prevalence of 3 percent in cirrhosis and 8 percent in cirrhotic ascites. The clinical situation is one of decompensated liver disease, usually cirrhosis, associated with the classic signs of portal hypertension including splenomegaly, esophageal varices and ascites. The latter is considered the sine qua non of the disease. Clinically, most patients have fever, abdominal pain, "peritoneal signs," impending hepatic coma and decreased or absent bowel sounds see Table (IV-10).

Laboratory findings include peripheral leukocytosis, abnormal values on liver function tests, positive blood cultures with the same organism as that found in the ascitic fluid (76 percent) and characteristic ascitic fluid changes. The ascitic fluid has the character of an "infected transudate." It is extremely rare to find the protein content of the ascitic fluid greater than 2.5 grams per 100 ml. This brings us to the question of what is "normal" ascites in regard to total cell count and differential count. Most authors have considered a total leukocyte count of less than 300 per cu mm and a polymorphonuclear (PMN) percentage of under 25 normal. Using these data, more than 90 percent of patients in a large series of patients with spontaneous peritonitis had an increased total leukocyte count (>300) and all had an increase in the PMN percentage in the ascitic fluid (>25 percent).[37]

The most commonly noted organisms cultured from infected ascites are E. coli followed by the pneumococcus, Klebsiella, enterococcus, streptococcus and Pseudomonas. It is extremely rare to find multiple or anaerobic organisms. Gram stain of the ascites is positive in about half the infected patients.

Regarding treatment, an immediate diagnostic paracentesis in all patients with ascites should be done. If the total leukocyte count is greater than 300 cells per cu mm or the percentage of PMN's is greater than 25 percent in an unstable patient with cirrhotic ascites, empirical antibiotic therapy appears to be indicated with penicillin and gentamicin pending the culture report. If more than one organism is isolated, a diagnostic search for a potential source of sepsis is indicated, such as diverticulitis with perforation. The same diagnostic evaluation is indicated if anaerobes are grown from the ascitic fluid, for as mentioned above, anaerobes do not appear to be associated with spontaneous peritonitis in patients with cirrhosis with any great frequency. Prognosis for this disease appears to be improving. In a 1971 report[37] only 3 percent of patients with SPC left the hospital while in a 1974 review[38] 20 percent were discharged, although the peritonitis was in fact arrested in about 60 percent in both series. This stresses the fact that these patients are extremely ill in addition to the peritonitis.

Tuberculous Peritonitis[39,40]

This is an unusual form of tuberculosis (Tbc), yet it is extremely important to identify. Most cases are due to reactivation of latent Tbc in the peritoneum established earlier at the time of hematogenous spread from a primary, usually pulmonary focus. Most patients with Tbc peritonitis do not have concurrent, active pulmonary, intestinal or genital Tbc. It is a disease usually seen in large municipal hospitals with their populations of pa-

tients with cirrhosis and poorly nourished and debilitated patients.

Clinically, Tbc peritonitis is an insidious disease presenting with fever, anorexia, weakness and weight loss. Ascites is found in almost all patients upon physical examination and more than half of the patients have complaint of abdominal pain which is usually diffuse in nature. The classically described "doughy" abdomen is rare. Intermediate purified protein derivative (PPD) skin test is virtually always positive if the process is not part of miliary Tbc. If miliary Tbc is present, 20 percent of patients will be anergic but a PPD test will be positive with successful therapy. An x-ray film of the chest may or may not be helpful.

The organism has been retrieved from the ascitic fluid about 80 percent of the time when more than 1 liter of ascitic fluid was cultured.[39] Results are poor when small amounts are cultured.[40] Blind peritoneal biopsy is positive in two thirds of cases and peritoneoscopy, with direct biopsy of the peritoneum, is strongly recommended when the diagnosis is suspected. The ascitic fluid characteristics ("Rule of 25's") which should make one consider Tbc peritonitis are the following: protein, greater than 2.5 grams per 100 ml; cells, greater than 250 cells per cu mm; lymphocytes, greater or equal to 75 percent (PMN's less than 25 percent).

Most authorities recommend triple therapy with isoniazid, ethambutol and streptomycin for three months, then discontinuing administration of streptomycin and continuing to give the other drugs for an additional 15 months. If the process was extremely indolent and long-standing before initiating therapy, corticosteroids may be added initially for three months and then tapered for six weeks and discontinued. The addition of corticosteroids is recommended by some authorities to prevent the development of adhesions at a later time with resulting intestinal obstruction and volvulus.

Fungal Peritonitis

Systemic candidiasis and histoplasmosis have been rarely reported to cause massive ascites and peritonitis by direct peritoneal involvement. This condition should be considered in the appropriate clinical setting, such as parenteral hyperalimentation or infected prosthetic heart valves.

Secondary Peritonitis

Bile Peritonitis

This condition usually arises after biliary surgical operation although traumatic, inflammatory and spontaneous perforations have been reported within the biliary tract. The diagnosis should be suspected in the appropriate clinical setting along with the suggestive chemical findings of a high conjugated bilirubin with a normal alkaline phosphatase determination.[41]

Bacterial Peritonitis

This condition results from a complication of a primary, usually serious, disease or injury of the abdominal cavity or its contents. The resulting peritonitis usually follows a perforation of the alimentary or genitourinary tract and is invariably polymicrobial with anaerobic organisms often predominating. The aerobic organisms commonly found include E. coli, Enterobacter, Streptococcus, Klebsiella, Pseudomonas, Proteus, Staphylococcus, Candida and diphtheroids. The anaerobic organisms include Bacteroides, Peptostreptococcus and Clostridium.

The aerobes and anaerobes seem to be synergistic in their pathogenic effect. Virulence appears to be greatly enhanced by the presence of devitalized tissue, blood products, irritants, foreign bodies and gastrointestinal enzymes.

Peritonitis secondary to biliary, gastroduodenal and activated pancreatic secretions is due to chemical irritation and inflammation for the first 12 to 24 hours, then subsequent bacterial invasion is responsible for the inflammatory process. Colonic injury with peritonitis was formerly considered to be more serious than upper gastrointestinal perforation because of the inability to control the anaerobes which reside in the large bowel, but at present small intestinal injury has a higher mortality rate because of the high concentration of gastrointestinal enzymes released into the abdominal cavity with resultant, aforementioned chemical inflammatory process of the peritoneum.

The topics of secondary peritonitis and intraabdominal abscesses are intimately related.[42] Table IV-11 lists, in approximate order of occurrence, the sources of intraabdominal abscesses. The discussion will be directed toward only the most prevalent conditions.

Peritonitis and abscess formation secondary to appendicitis.[43] Obstruction and infection are the

TABLE IV-11.—*Intraabdominal Abscesses—Source*

Appendicitis
Pancreatitis
Genitourinary
Biliary
Diverticulitis
Perforated ulcer (peptic vs. infectious)
Inflammatory bowel (granulomatous, ulcerative colitis)
Ischemic bowel
Osteomyelitis
Amebiasis, Actinomycosis

two factors which are most important in the pathogenesis of human appendicitis. Obstruction leads to an increase in intraluminal pressure producing interference with venous outflow which results in thrombosis, hemorrhage, edema and bacterial invasion of the wall of the appendix.

The classic clinical sequence of events seen in acute appendicitis are upper abdominal pain migrating to the right lower quadrant (which is seen in only half of patients), followed by anorexia, nausea and vomiting, and then fever. In only 10 percent of patients are appendoliths seen on plain films of the abdomen. Positive findings on an abdominal film combined with an appropriate history and physical virtually assures the diagnosis. Other x-ray findings are a sentinel loop in the right lower quadrant, obliteration of the right psoas shadow, gas bubbles in the right lower quadrant (with perforation) and gas in the appendix. The latter is rarely noted in normal persons.

Peritonitis is found in a third of all cases at surgical operation but in patients over 60 years old this figure rises to 70 percent. Perforation with peritonitis is suspected when there is increasing abdominal tenderness over a widening area with high fever and leukocytosis. Late findings include abdominal distention and vascular collapse. The infection is polymicrobial and usually three to seven organisms are isolated. For stable patients with the findings of a local right lower quadrant abscess or a clinical history of a perforated appendix five or more days previously, management consists of nasogastric suction, therapy with antibiotics (gentamicin and clindamycin), correction of fluid and electrolyte disorders, and bedrest. A well localized abscess can be drained extraperitoneally, such as through the rectum. After the inflammation has subsided, the appendix should be removed at the earliest possible time. When surgical operation is done, aspiration of pus and drainage of appropriate areas of the abdomen are carried out—that is, cul-de-sac, right paracolic gutter and the involved area of the caecum. Peritoneal lavage with antibiotics is not recommended because of peritoneal irritation and dissemination, and moreover preoperative use of antibiotics makes lavage unnecessary.

Diverticulitis with perforation.[44] Diverticulitis by our definition means perforation of a diverticulum, not only an inflammation within a diverticulum. Perforation may be generalized or local with abscess formation. The abscess may surround the colon and cause obstruction, or the abscess may burrow into adjacent organs—uterus, vagina, small intestine, bladder or abdominal wall—and may, therefore, mimic Crohn's disease of the colon. The typical attack of diverticulitis is characterized by left lower quadrant pain, chills, fever and peritoneal signs. A tender mass over the sigmoid may be palpated. (It should be noted that left lower quadrant pain and a mass in this area may be secondary to diverticulosis with pronounced muscular hypertrophy.) One should make the diagnosis of diverticulitis when fever, chills and leukocytosis are associated with the above physical findings. Findings on analysis of urine may be abnormal due to contiguous involvement of the bladder or left ureter by a pericolic abscess.

Proctoscopic examination may be done to exclude other disorders (for instance, Crohn's disease) but should be done without preparation and without air insufflation. A limited barium enema using anticholinergics with a water soluble material may be done if the diagnosis is in doubt. A word of caution: do not use morphine or codeine for analgesia. Both drugs can dramatically raise the pressure within the involved colon. Meperidine does not share this property with morphine.

Therapy may be medical in a patient who is unsuited for immediate surgical operation, or for a patient in whom this is the first episode of diverticulitis and there is dramatic response to nonoperative therapy. If clinical deterioration occurs or if the mass appears to be enlarged while being treated medically, immediate surgical intervention is indicated. Surgical operation for diverticulitis with perforation should be a three-staged procedure:

- Drain abscess, close perforation and carry out proximal colostomy.
- Resect involved area with end to end anastomosis.
- Close colostomy.

If a definitive resection is attempted initially in an area of suppuration, great morbidity will be seen—such as fistulae or anastomotic breakdown.

Gastroduodenal perforations. Approximately 5 percent of peptic ulcers perforate at some time. The ratio of duodenal to gastric ulcers that perforate is 15:1, whereas the ratio of duodenal to gastric ulcers in incidence is 5:1. Most are free perforations into the peritoneal cavity. The initial presentation is that of a dramatic chemical peritonitis with the patient having a board-like abdomen and early shock. Hours later a deceptive improvement occurs in many patients as a result of dilution and neutralization of gastroduodenal contents. This is followed by signs of general, now bacterial, peritonitis. The mortality rate for untreated perforated peptic ulcer doubles after eight hours, emphasizing the need for early diagnosis and treatment.

Treatment in most instances is immediate surgical operation. Exceptions to this rule include those patients in whom the perforation is rapidly sealed off by omentum or viscera. In this case, nasogastric suction for two to three days and administration of fluids and antibiotics may be tried. Any suggestion of increasing peritoneal signs or clinical deterioration should prompt immediate surgical procedures. The second possibility for nonoperative therapy of a free ulcer perforation may be made in the management of patients with another grave illness which would significantly increase surgical mortality, such as myocardial infarction or respiratory failure. Most surgeons now favor doing a definitive acid-lowering procedure during the emergency operation. In two thirds of patients treated by simple closure additional definitive surgical procedures for ulcer will be needed within five years. Definitive acid-lowering procedures currently recommended are either vagotomy and drainage or vagotomy and antrectomy with closure of the perforation.

Pancreatitis with abscess.[45] Acute pancreatitis with the initial chemical peritonitis secondary to the release of pancreatic enzymes is a familiar clinical entity. In 4 percent of patients with acute pancreatitis a secondary pancreatic abscess develops. Untreated pancreatic abscesses are almost uniformly fatal. Bacteria are cultured from over 90 percent of these abscesses. This complication usually occurs one to four weeks after initial improvement in a patient with pancreatitis. The origin of bacterial contamination of the pancreas is unknown but is most likely due to direct transmural penetration from the transverse colon which is usually involved concomitantly with the acute pancreatic inflammatory process. The abscess may spread from the lesser sac to the subphrenic spaces (left or right) or even rarely dissect into the mediastinum, transverse colon, sigmoid, psoas or scrotum.

For diagnosis, unfortunately, amylase elevations are inconsistent and blood cultures may or may not be positive. Usually an upper gastrointestinal series or barium enema (or both) is needed to define a retrogastric mass. Abdominal sonography has become a useful diagnostic approach in evaluating pancreatic pseudocysts and abscesses. Therapy for this disease entity has been somewhat disappointing.

Although spontaneous drainage of the abscess into an adjacent viscus does occur, it is inadequate therapy. However, even with adequate prompt surgical drainage of the abscess, there is a 33 percent mortality rate. It should be noted that use of prophylactic antibiotics during pancreatitis does not prevent the subsequent occurrence of an abscess and may even lead to the selection of resistant organisms.

Typhoid ulceration and peritonitis. Typhoid fever may be complicated by peritonitis. Involved Peyer's patches may undergo necrosis and ulceration with perforation. Sudden development of severe localized pain in the right lower quadrant in a patient with typhoid during the second or third week of illness suggests the diagnosis. If leukopenia is present, it may convert to a sudden pronounced leukocytosis. Rapid surgical intervention is indicated with resection of the involved bowel under proper antibiotic coverage.

Tuberculous ulcers with bacterial peritonitis. Tuberculosis (Tbc) of the intestine is at times clinically and radiologically indistinguishable from Crohn's disease. Rarely, free perforation may complicate Tbc of the terminal ileum and caecum. Treatment would include immediate segmental resection along with anti-Tbc therapy and antibiotics for the resulting bacterial peritonitis.

Ulcerative, granulomatous and amoebic colitis. Toxic megacolon occurring in a patient with the above conditions carries a high mortality and is usually associated with multiple microperforations of the colon. The resulting peritonitis is bacterial in cause.

Nonperforated lesions of the gastrointestinal tract associated with peritonitis. Intestinal obstruction, volvulus, intussusception and ichemia

of either the small intestine or colon will result in increased permeability of the bowel wall with subsequent peritonitis. Surgical treatment of the underlying process is essential in order to contain the subsequent peritonitis.

TRADE AND GENERIC NAMES OF DRUGS

Cleocin® ..... *clindamycin HCl*
Lincocin® ..... *lincomycin*
Achromycin®, Panmycin®,
Tetracyn® ..... *tetracycline HCl*
Polycillin®, Omnipen®, Totacillin®,
Amcil®, Penbritin®, Principen® ..... *ampicillin*
Flagyl® ..... *metronidazole*
Emetine HCl ..... *emetine HCl*
Aralen® phosphate ..... *chloroquine phosphate*
Diiodohydroxyquin ..... *diiodohydroxyquin*
Chloromycetin® ..... *chloramphenicol*
Bactrim®, Septra® .... *trimethoprim-sulfamethoxazole*
Lomotil® .... *diphenoxylate HCL with atropine sulfate*
Gastrografin® ..... *meglumine diatrizoate*
Penicillin G ..... *penicillin G*
Garamycin® ..... *gentamicin*
INH®, Triniod®, Nydazid® ..... *isoniazid*
Myambutol® ..... *ethambutol*
Streptomycin ..... *streptomycin*
Morphine ..... *morphine*
Codeine phosphate ..... *codeine phosphate*
Demerol®, Mepergan® ..... *meperidine HCl*
Vancocin® ..... *vancomycin*
Indocin® ..... *indomethacin*

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